

REMARKS

Claims 1, 2, 7, 12, 14-44, 46-53, 62, 67-75, 82-83, 88, 90, 97, 99, 102, 104, 106 and 108-110 are pending in the instant application. In paragraph 2 of the outstanding Office Action (Paper No. 11), the Examiner has noted that while Applicants intended to cancel non-elected claims 35, 38, 52-53, 62, 67-75, 82-83, 88, 90, 97, 99, 102, 104, 106 and 108 in the previous response (Applicants' REMARKS in Paper No. 10), no amendment was submitted directing cancellation of said claims. Applicants have directed cancellation of said claims in the instant amendment in order to clarify the record. Applicants' cancellation of claims should in no way be construed as an acquiescence to the restriction of claims required in Paper No. 10. Applicants traverse any supplemental restriction of claims 35, 38, 52-53, 62, 67-75, 82-83, 88, 90, 97, 99, 102, 104, 106 and 108 as well as the restriction of the remaining pending claims for reasons set forth below. Applicants reserve the right comment more fully on the reasons for traversal of the restriction of any cancelled claims and to pursue the claims as originally filed in this or in a separate application(s).

The claims of the instant application were first subject to a Restriction Requirement in Paper No. 7, mailed from the Patent Office on December 3, 2001. In that communication, the Examiner required restriction to one of five inventions under 35 U.S.C. 121, namely

- methods of making panto-compounds in microorganisms *in vivo* (Group I),
- methods of producing panto-compounds *in vitro* (Group II),
- methods for identifying modulators of pantothenate kinase (Group III),
- modified microorganisms (Group IV), and
- pantothenate biosynthetic enzymes (Group V).

Within each group, the Examiner identified generic claims and noted several patentably distinct species requiring election of one species for prosecution on the merits. Applicants elected Group I (claims 1, 2, 7, 12, 14-34, 36, 37, 39-44 and 46-51) and within the group, elected the species featuring microorganisms having deregulated

ketopantoate reductase (*panE*) for prosecution purposes (the claims readable upon the elected species include claims 1-2, 7, 12, 19, 24, 26-28, 33-34 and 48-51). This species election was made based on the understanding that upon the allowance of a generic claim, Applicants would be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. Applicants did not traverse the previous Restriction Requirement (Paper No. 7).

A supplemental Restriction Requirement has now been mailed from the Patent Office (Paper No. 11), in which restriction to one of the following inventions is required under 35 U.S.C. 121:

- Group I: Claim(s) 1, 2, 7, 12, 14-20, 24-29, 33-35, drawn to a method of producing panto-compound comprising culturing a microorganism that overexpresses a *Bacillus* or *Bacillus subtilis* pantothenate biosynthetic enzyme, a method of producing pantothenate in a manner independent of precursor feed by culturing a microorganism overexpressing aspartate-alpha-decarboxylase having a deregulated isoleucine-valine (*ilv*) pathway, overexpressing acetohydroxyacid synthetase encoded by an *ilvBN* nucleic acid sequence, and overexpressing ketopantoate reductase encoded by a *panE1* nucleic acid sequence, classified in class 435, subclass 129;
- Group II: Claim(s) 1, 2, 7, 12, 14-20, 24-29, 33-35, drawn to a method of producing a panto-compound comprising culturing a microorganism that overexpresses a *Bacillus* or *Bacillus subtilis* pantothenate biosynthetic enzyme, a method of producing pantothenate in a manner independent of precursor feed by culturing a microorganism overexpressing aspartate-alpha-decarboxylase having a deregulated *ilv* pathway, transformed with a vector comprising an *alsS* nucleic acid sequence encoding acetolactate synthase, and overexpressing ketopantoate reductase encoded by a *panE1* nucleic acid sequence, classified in class 435, subclass 129;
- Group III: Claim(s) 1, 2, 7, 12, 14-19, 21, 24-28, 30, 33-35, drawn to a method of producing a panto-compound comprising culturing a microorganism that overexpresses a *Bacillus* or *Bacillus subtilis* pantothenate biosynthetic enzyme, a method of producing pantothenate in a manner independent of precursor feed by culturing a microorganism overexpressing aspartate-alpha-

decarboxylase having a deregulated *ilv* pathway and overexpressing acetohydroxyacid isomeroreductase encoded by an *ilvC* nucleic acid sequence, and overexpresses ketopantoate reductase encoded by a *panE1* nucleic acid sequence, classified in class 435, subclass 129.

- Group IV: Claim(s) 1, 2, 7, 12, 14-19, 22, 24-28, 31, 33-35, drawn to a method of producing a panto-compound comprising culturing a microorganism that overexpresses a *Bacillus* or *Bacillus subtilis* pantothenate biosynthetic enzyme, a method of producing pantothenate in a manner independent of precursor feed by culturing a microorganism overexpressing aspartate-alpha-decarboxylase having a deregulated *ilv* pathway, overexpressing dihydroxyacid dehydratase encoded by an *ilvD* nucleic acid sequence, and overexpressing ketopantoate reductase encoded by a *panE1* nucleic acid sequence, classified in class 435, subclass 129;
- Group V: Claim(s) 1, 2, 7, 12, 14-19, 23, 24-28, 32-35, drawn to a method of producing a panto-compound comprising culturing a microorganism that overexpresses a *Bacillus* or *Bacillus subtilis* pantothenate biosynthetic enzyme, a method of producing pantothenate in a manner independent of precursor feed or independent of aspartate or beta-alanine feed by culturing a microorganism overexpressing aspartate-alpha-decarboxylase having a deregulated *ilv* pathway, transformed with a vector comprising a *panD* nucleic acid sequence encoding aspartate-alpha-decarboxylase, and overexpressing ketopantoate reductase encoded by a *panE1* nucleic acid sequence, classified in class 435, subclass 129;
- Group VI: Claim(s) 1, 2, 14-20, 24-29, 33-35, drawn to a method of producing a panto-compound comprising culturing a microorganism that overexpresses a *Bacillus* or *Bacillus subtilis* pantothenate biosynthetic enzyme, a method of producing pantothenate in a manner independent of precursor feed by culturing a microorganism overexpressing aspartate-alpha-decarboxylase having a deregulated isoleucine-valine (*ilv*) pathway, overexpressing acetohydroxyacid synthetase encoded by an *ilvBN* nucleic acid sequence, and overexpressing ketopantoate hydroxymethyltransferase (*panB*) and pantothenate synthetase (*panC*) or transformed with a *panBCD* nucleic acid sequence, classified in class 435, subclass 129;
- Group VII: Claim(s) 1, 2, 14-20, 24-29, 33-35, drawn to a method of producing a panto-compound comprising culturing a

microorganism that overexpresses a *Bacillus* or *Bacillus subtilis* pantothenate biosynthetic enzyme, a method of producing pantothenate in a manner independent of precursor feed by culturing a microorganism overexpressing aspartate-alpha-decarboxylase having a deregulate *ilv* pathway, transformed with a vector comprising an *alsS* nucleic acid sequence encoding acetolactate synthase, and overexpressing ketopantoate hydroxymethyltransferase (*panB*) and pantothenate synthetase (*panC*) or transformed with a *panBCD* nucleic acid sequence, classified in class 435, subclass 129;

Group VIII. Claim(s) 1, 2, 14-19, 21, 24-28, 30, 33-35, drawn to a method of producing a panto-compound comprising culturing a microorganism that overexpresses a *Bacillus* or *Bacillus subtilis* pantothenate biosynthetic enzyme, a method of producing pantothenate in a manner independent of precursor feed by culturing a microorganism overexpressing aspartate-alpha-decarboxylase having a deregulated *ilv* pathway and overexpressing acetohydroxyacid isomeroreductase encoded by an *ihc* nucleic acid sequence, and overexpresses ketopantoate hydroxymethyltransferase (*panB*) and pantothenate synthetase (*panC*) or transformed with a *panBCD* nucleic acid sequence, classified in class 435, subclass 129.

Group IX: Claim(s) 1, 2, 14-19, 22, 24-28, 31, 33-35, drawn to a method of producing a panto-compound comprising culturing a microorganism that overexpresses a *Bacillus* or *Bacillus subtilis* pantothenate biosynthetic enzyme, a method of producing pantothenate in a manner independent of precursor feed by culturing a microorganism overexpressing aspartate-alpha-decarboxylase having a deregulate *ilv* pathway and overexpressing dihydroxyacid dehydratase encoded by an *ilvD* nucleic acid sequence, and overexpresses ketopantoate hydroxymethyltransferase (*panB*) and pantothenate synthetase (*panC*) or transformed with *panBCD* nucleic acid sequence, classified in class 435, subclass 129.

Group X: Claim(s) 1, 2, 14-19, 23, 24-28, 32-35, drawn to a method of producing a panto-compound comprising culturing a microorganism that overexpresses a *Bacillus* or *Bacillus subtilis* pantothenate biosynthetic enzyme, a method of producing pantothenate in a manner independent of precursor feed or independent of aspartate or beta-alanine feed by culturing a microorganism overexpressing aspartate-alpha-decarboxylase having a deregulated *ilv* pathway, transformed with a vector

comprising a *panD* nucleic acid sequence encoding aspartate-alpha-decarboxylase, and overexpresses ketopantoate hydroxymethyltransferase (*panB*) and pantothenate synthetase (*panC*) or transformed with a *panBCD* nucleic acid sequence, classified in class 435, subclass 129;

- Group XI: Claim(s) 36-38, drawn to a method of producing beta-alanine by culturing a microorganism overexpressing aspartate-alpha-decarboxylase and having a mutation in a nucleic acid encoding ketopantoate hydroxymethyltransferase, classified in class 435, subclass 116;
- Group XII: Claim(s) 39-44, 46, 47, 50, 51, drawn to a method for enhancing production of a panto-compound by culturing a microorganism having a mutant pantothenate kinase encoded by a mutant *coaX* and *coaA* genes, classified in class 435, subclass 129;
- Group XIII: Claim(s) 41, 46, 47, 48, 50, 51, drawn to a method for enhancing production of a panto-compound by culturing a microorganism having a mutant pantothenate kinase and having a deregulated *ilv* biosynthetic pathway, classified in class 435, subclass 129;
- Group XIV: Claim(s) 41, 42, 46, 47, 49, 50, 51, drawn to a method for enhancing production of a panto-compound by culturing a microorganism having a mutant pantothenate kinase and overexpressing *panD* encoding aspartate-alpha-decarboxylase and *panE* encoding ketopantoate reductase, classified in class 435, subclass 129;
- Group XV: Claim(s) 52, 53, drawn to a method for identifying compounds that modulate pantothenate kinase activity by contacting a cell expressing pantothenate kinase encoded by *coaX* gene and a *coaA* gene, classified in class 435, subclass 15;
- Group XVI: Claim(s) 62, 67-69, 71-75, 83, 88, 99, 108, drawn to a recombinant microorganism overexpressing a *Bacillus* pantothenate biosynthetic enzyme, a nucleic acid molecule comprising a mutant *coaX* gene, a vector comprising a mutant *coaX* nucleic acid, a recombinant microorganism having mutant *coaX* and *coaA* genes, classified in class 435, subclass 252.31;
- Group XVII: Claim(s) 70, 83, 90, 99, 109, drawn to a nucleic acid comprising *coaX* gene, a vector comprising a *coaX* said nucleic acid, classified in class 536, subclass 23.2;

- Group XVIII: Claim(s) 82, drawn to a recombinant microorganism, classified in class 435, subclass 252.31;
- Group XIX: Claim(s) 83, 97, drawn to a vector, classified in class 435, subclass 320.1;
- Group XX: Claim(s) 102, 104, drawn to a *Bacillus* ketopantoate reductase polypeptide, classified in class 435, subclass 190;
- Group XXI: Claim(s) 102, 106, drawn to a *Bacillus* aspartate-alpha decarboxylase polypeptide, classified in class 435, subclass 232;
- Group XXII: Claim(s) 102, 110, drawn to an isolated pantothenate kinase protein encoded by a *coaX* gene, classified in class 435, subclass 194.

Applicants traverse. It is Applicants' position that the instant Examiner has improperly restricted the claims under 35 U.S.C. 121. In particular, it is Applicants' position that the Examiner has improperly characterized the claimed subject matter as relating to twenty-two (22) distinct inventions when in fact, the claims are directed to a much smaller number of generic inventions including patentably distinct species, as set forth in the previous Restriction Requirement (Paper No. 7). It is further Applicants' position that searches of the subject matter of the above 22 groups would be necessarily coextensive and there would be no undue burden on the Examiner to search the subject matter of the groups as originally set forth in the previous Restriction Requirement (Paper No. 7).

In a telephonic interview with the Examiner held January 23, 2003, including the undersigned and Elizabeth A. Hanley (Reg. No. 33,505), Applicants position was discussed. The Examiner agreed to hold another telephonic interview including the above and the Examiner's supervisor to further discuss the merits of the instant Restriction Requirement. The undersigned intends to arrange such an interview as soon as the supervisor's schedule permits.

Applicants are in agreement with the record to extent that the claims be grouped as set forth in the previous Restriction Requirement (Paper No. 7). Applicants' traversal

is to the supplemental Restriction Requirement. However, in order to be fully responsive to the outstanding Office Action, Applicant hereby elects Group XIV for prosecution in the present application with traverse. Applicants note that Group XIV includes claims featuring microorganisms having deregulated ketopantoate reductase (*panE*), which is consistent with Applicants election of the invention of Group I and election of species for prosecution purposes made in Paper No. 11.

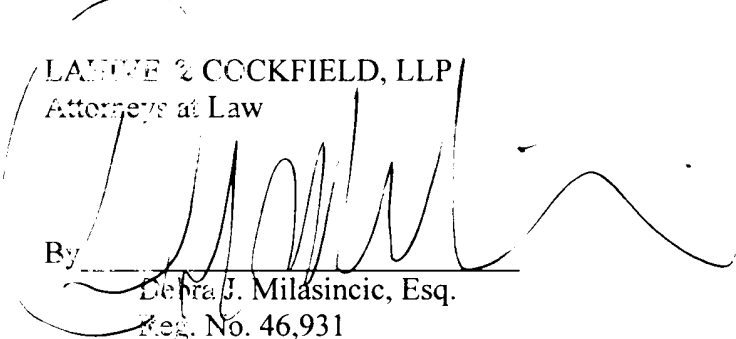
SUMMARY

Pending our next telephonic interview, if a telephone conversation with Applicants' Attorney would expedite the prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 227-7400.

Date: January 27, 2003

LAWFEE & COCKFIELD, LLP
Attorneys at Law

By


Debra J. Milasincic, Esq.

Reg. No. 46,931

Attorney for Applicants

28 State Street

Boston, MA 02109

(617) 227-7400

(617) 742-4214